FALSIFICATION OF CHLOROQUINE ANTIMALARIALS: REALITIES AND METHODS OF DETECTION

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Introduction. Up to two billion people around the world lack access to necessary medicines, vaccines, medical devices including in vitro diagnostics, and other health products, which creates a vacuum that is too often filled by substandard and falsified products. This problem is growing as global supply chains become more complex, meaning products manufactured in one country may be packaged in a second country and distributed across borders to be marketed or sold to consumers in a third. The growth of e-commerce also contributes to this trend by making it easier to purchase medicines online, often from unauthorized sources.

The World Health Organization (WHO) has identified this issue as one of the urgent health challenges for the next decade, given that more than one in ten medicines in low- and middle-income countries are estimated to be substandard or falsified. No country remains untouched from this issue, and WHO has received reports of substandard or falsified medical medicines, vaccines and in vitro diagnostics from all regions of the world. Both generic and innovator medicines can be falsified, ranging from costly products for cancer to very inexpensive products for treatment of pain.

Antimalarial medicines, such as chloroquine drugs, are among the most reported substandard and falsified medical products (9.5% of all antimalarials) in countries of Africa, Asia and even Europe. Among the medicines that were subject to counterfeiting were chloroquine drugs, which were distributed worldwide, including to Burkina Faso, Cameroon, Democratic Republic of Congo, France, and Niger.

Aim. To consider the problem of falsification of chloroquine medicines and to select methods for the tasks of forensic pharmaceutical research.

Materials and methods. For this case study, we reviewed WHO reports on substandard or falsified medicines and documents from judicial and pharmaceutical cases on methods for determining chloroquine in medicines that are suspected of being falsified.

Results and discussion. Chloroquine phosphate or sulfate is referenced on the WHO Model List of Essential Medicines for the treatment of Plasmodium vivax infection (malaria). Large clinical trials are under way to generate the robust data needed to establish the efficacy and safety of chloroquine and hydroxychloroquine in the treatment of COVID-19. These medicines are currently authorized for malaria and certain autoimmune diseases, and it is important that patients do not face shortages caused by stockpiling or use outside the authorized indications. Both chloroquine and hydroxychloroquine can have serious side effects, especially at high doses or when combined with other medicines.

Therefore, to ensure the circulation of quality, safe and effective chloroquine tablets with consistent and predictable therapeutically active pharmaceutical ingredients, such quality assessment studies are necessary tools. Because they can provide an insight into the quality of these products circulated within the distribution chain and consumed and at the same time, they may give a clue to therapeutic success/failure of malaria management. They may generate base-line evidence either to develop and endorse optimum specifications and standards, encourage and enforce their application or for preventive, corrective measures to be taken by drug regulatory authorities. With the objective of assessing physicochemical quality parameters of chloroquine phosphate tablets circulating in

Africa by confirming whether they comply with the Pharmacopoeia specifications and whether origin, collection site and manufacturers have an impact on the tested products quality.

A Liquid chromatography method with a 4.6 mm ×15 cm, with a 5-µm packing L1 column that is adjusted in a 224 nm detector is used. A mobile phase is prepared by mixing buffer (water, monobasic potassium phosphate, and perchloric acid) and methanol in a 78:22 ratio and degassing it. The flow rate and injection volume used for assay are 1.2 mL/minute and 10 µL, respectively.

For analysis is used the sample with nominally 7.5 mg of chloroquine phosphate from the finely powdered tablet is transferred to a 50 mL volumetric flask and dissolved in and diluted with a volume. The solution then sonicates for 20 mins. Using a nylon filter of 0.2-µm pore size,10mL of the solution can pass, discarding the first 4mL, 2mL of the filtrate is used for analysis. The obtained results are compared with the spectrum of the standard sample.

The thin-layer chromatography method can be proposed to determination of chloroquine in forensic and pharmaceutical analysis. The analysis is carried out using ready-to-use TLC plates, silica gel 60F (20 × 20 cm). These plates are placed in glass vats with mobile phase 1.5 mL of 25% ammonia, 20 mL of methanol and 80ml of chloroform. 10 µL of 10 mg/mL solution of sample in acetic acid and reference solution in the same concentration are deposited using a micropipette on the plate (previously activated) 2 cm from the bottom edge on the baseline. Each deposit is dried. The plate is then placed in the migration chamber containing the mobile phase. When the solvent front reached 1 cm from the upper edge of the plate, the chromatograms are removed, dried and viewed in the UV lamp at 254 nm and then using iodine steam.

Conclusions. The study considered that the antimalarial drug chloroquine is massively falsified in Africa, Asia and some European countries, which is a global problem for the pharmaceutical and medical industries. Therefore, we have reviewed and proposed accurate, specific methods for determining chloroquine in cases of suspected counterfeiting. For this purpose, we have proposed a liquid chromatography method and a thin-layer chromatography method that allow the determination of chloroquine both in mono-component medicines and in combinations with other active pharmaceutical ingredients.

MODERN METHODS OF ANALYSIS IN THE FOOD INDUSTRY

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Introduction. In food production, the quality and the composition of the raw material, the efficiency of production processes, environmental safety, compliance of products with the established standards and with sanitary and hygienic requirements are very important. Most of the methods described are now used in the analysis of both food products and pharmaceutical substances.

Aim. The aim of our research was to study modern methods of analysis used in the food industry, as well as in the analysis of dietary supplements; to assess the advantages and disadvantages of classical and modern methods of analysis, and trends in their development.

Materials and methods. The periodicals and electronic publications available to us over the past ten years were critically reviewed, and an attempt was made to perform a comparative analysis of modern analytical methods of analysis used in the food industry.